



TITLE:

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CONSERVATIVE MANAGEMENT OF SMALL RENAL TUMORS

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With the widespread use of imaging modalities, incidentally discovered small renal cell carcinomas have increased. Some patients, however, are too old or weak due to various diseases to undergo surgery and other patients occasionally refuse surgery. To investigate the natural history of small renal cell carcinoma, we retrospectively reviewed patients with small renal tumors suggestive of carcinoma. We retrospectively reviewed 15 patients with contrast-enhancing renal masses less than 4.0 cm in diameter who were observed without treatment. The mean follow-up period was 38 months (range, 8–91). The average patient age was 67 years (range, 44–87). The initial average tumor diameter was 2.2 cm (range, 1.0–3.9). The average growth rate was 0.06 cm per year (range, –0.09–0.28). Only 4 tumors grew obviously during the follow-up period. Three tumors were removed surgically by radical nephrectomy, and all tumors were pathologically diagnosed as renal cell carcinoma. None of the patients developed metastases during the follow-up period or after surgery. Two patients died of other causes. Nonsurgical watchful waiting may be an acceptable treatment option for elderly or severely comorbid patients; however, it is not known whether this conservative management can be applied to young or otherwise healthy patients.

(Hinyokika Kyo **53** : 207–211, 2007)

Key words : Renal neoplasm, Growth rate, Natural history, Follow-up studies, Surveillance

INTRODUCTION

With the widespread use of modern imaging modalities for mass screening or other diseases, incidentally discovered renal cell carcinomas (RCCs) have increased^{1–2}.

Most patients are treated surgically soon after diagnosis. Some patients, however, are too old or weak due to various diseases to undergo surgery and other patients occasionally refuse surgery. Recent minimally invasive treatments such as radiofrequency ablation and cryotherapy are not available everywhere and their long-term efficacy has not yet been confirmed^{3–6}. The natural history of RCCs has not been investigated thoroughly, and yet it is well known that small RCCs rarely metastasize and have a slow growth rate^{7–12}. Thus, watchful waiting is an attractive treatment option in elderly or comorbid patients. To investigate the natural history of small renal cell carcinoma, we reviewed patients with small renal tumors suggestive of carcinoma who were observed without treatment, including surgery.

PATIENTS AND METHODS

We retrospectively reviewed the records of 15 patients (13 men and 2 women) who had contrast-enhancing solid renal masses less than 4.0 cm in greatest diameter discovered from March 1997 to August 2004 (Table 1). All tumors were assumed to be renal cell carcinoma

based on imaging characteristics. All tumors were found incidentally during mass screening or a routine examination for other diseases. Tumor diameter was determined by measuring the maximum axial diameter of each lesion on periodic CT images. Most examinations were performed using 5-mm-thick sections, although some examinations were performed with 10-mm-thick sections. They were followed with serial abdominal CT imaging using various types of equipment.

The average age of the 15 patients at initial diagnosis was 67 years (range, 44–87 years). All patients were asymptomatic. One patient was treated with chronic intermittent hemodialysis for chronic glomerulonephritis. The mean follow-up period was 38 months (range, 8–91 months). The median number of tumor measurements per patient was 5 (range, 2–19). The mean baseline tumor diameter was 2.2 cm (range, 1.0–3.9 cm).

The reasons for watchful waiting were patient's wishes (n=9), severe comorbidity unsuitable for surgery (n=3), initially indeterminate mass (n=1), and concomitant incurable carcinomas (n=2). Of the nine patients who requested watchful waiting, eight had relatively severe medical comorbidity such as cerebral infarction, respiratory insufficiency and heart failure. Severe comorbidities unsuitable for surgery were chronic heart failure (n=2) and acute peritonitis for duodenal ulcer perforation (n=1). Incurable carcinomas (lung and hepatic cancer) were diagnosed and treated before renal tumors were discovered.

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Table 1. The patient characteristics and outcome

No.	Age/Sex	Initial tumor size (cm)	Final tumor size (cm)	Followup (month)	Growth rate (cm/year)	Outcome
1	76/M	1	1	15	0	Alive and well
2	49/M	1	2.2	53	0.27	Alive and well
3	80/M	1.2	1.2	29	0	Alive and well
4	71/M	1.6	2.1	67	0.09	Alive and well
5	75/M	3.2	3.2	33	0	Alive and well
6	75/F	3.2	3.2	14	0	Alive and well
7	44/M	3	3	14	0	Surgery, no evidence of disease
8	77/F	3.9	4.2	13	0.28	Alive and well
9	82/M	1.5	3.1	91	0.21	Alive and well
10	72/M	2.6	2	79	-0.09	Dead from other causes
11	50/M	1.5	1.5	12	0	Surgery, no evidence of disease
12	87/M	3.5	3.5	37	0	Alive and well
13	71/M	2.5	2.5	60	0	Dead from other causes
14	59/M	1	1	44	0	Alive and well
15	42/M	2	2	8	0	Surgery, no evidence of disease
Average	67	2.2	2.4	38	0.06	

Table 2. Summary of previously reported cases describing the growth rate of small renal tumors

Reference	Year	No. Pts/No. tumors	Mean age	Initial tumor size (cm)	Follow-up (month)	Growth rate (cm/year)	No. Surgery/Total No.
Whele, et al. ⁷⁾	2004	29/29	70	1.83 (0.4-3.5)	32.0	0.12	6/32
Rendon, et al. ⁸⁾	2000	13/13	69	2.95 (0.9-4.0)	42.0	0.216	5/13
Volpe, et al. ⁹⁾	2004	29/32	71	2.48 (0.9-3.9)	27.9	0.1	9/32
Bosniak, et al. ¹⁰⁾	1995	37/40	65.5	1.48 (0.2-3.5)	39.0	0.36	26/40
Kato, et al. ¹¹⁾	2004	18/18	56.5	2.0 (1.0-3.4)	22.5	0.42	18/18

RESULTS

The mean tumor diameter at the last measurement was 2.4 cm. The average growth rate was 0.06 cm per year (range, -0.09-0.28). Only 4 cases grew obviously during the follow-up period. The diameter of one tumor decreased, but those of the other 9 cases did not increase at all during the follow-up period.

Three tumors were removed surgically by radical nephrectomy and have not grown at all during the observation period. One tumor (case 7) was removed 14 months after diagnosis. Although he was unsuitable for surgery because of his medical condition at initial diagnosis, his condition improved enough to perform the operation. One patient (case 11) had an initially indeterminate mass, but RCC was confirmed by percutaneous biopsy 12 months after initial diagnosis. One tumor (case 15) was detected by abdominal CT for acute abdomen. The patient was diagnosed with perforation of the duodenum due to peptic ulcer and treated surgically. Eight months later the tumor was removed. All tumors were pathologically diagnosed as clear cell carcinoma. The tumors were graded on a scale of 1-3 based on nuclear appearance according to the International Union Against Cancer (UICC) TNM classification with minor modifications advocated by the

Japanese Urological, Pathologic and Radiological Societies¹³⁾. One RCC was classified as Grade 1, and the remaining 2 RCCs were classified as Grade 2; none of the patients were classified as Grade 3.

Two patients died of liver and lung cancer. None of the patients developed metastases during the follow-up period or after surgery.

DISCUSSION

With the widespread use of imaging modalities for mass screening or other diseases, incidentally detected RCCs have increased¹⁻²⁾. Most patients are treated surgically soon after diagnosis; however, surgical extirpation cannot be applied to some patients for various reasons. If the tumor grows slowly and metastatic potential is low, watchful waiting is an attractive treatment option for these patients.

Recent minimally invasive therapies, such as radiofrequency ablation and cryotherapy may offer treatment options for patients unsuitable for surgery³⁻⁶⁾. The incidence of complications with these treatments and damage to patients is less than with the standard treatment¹⁴⁾. Good short-term efficacy is reported with these treatments³⁻⁶⁾; long-term efficacy, however, has not yet been established. Moreover, these treatments are still not easy to access in Japan, but they will become

popular and good treatment options for elderly or comorbid patients in Japan in the near future.

Small RCCs (3–4-cm diameter or less) rarely develop metastases and the prognosis is good¹²⁾. The size of the primary tumor is generally large when patients have metastases. Some reports showed that high-grade tumors grew faster than low-grade tumors^{10–11)}, so high-grade tumors are rarely discovered when tumors are small. The natural characteristics, such as the growth rate and metastatic potential, of high-grade tumors may be different from low-grade tumors. Only 1 or 2 cases of high-grade tumors have been found in previously reported series that followed RCCs without treatment. In our cases, all 3 tumors resected were likewise histologically diagnosed as Grade 1 or 2.

Reports have shown that 68–88% of small solid contrast-enhancing renal tumors are RCC, and the rest are oncocytoma^{12,15)}, but this percentage may need to be revised downward as the mass size decreases. In our cases, all 3 resected tumors were pathologically diagnosed as RCC. Of the remaining 12 tumors, only 1 or 2 benign tumors were possibly included; however, in three operated patients, the follow-up period was relatively shorter than in not pathologically diagnosed patients. So it is not known whether the natural characteristics and growth rate of resected tumors are similar to those of observed tumors without treatment.

If tumors are histologically diagnosed as benign by percutaneous biopsy, they can be observed safely without further treatment. Histological diagnosis, however, using needle biopsy specimens, is not always accurate¹⁶⁾ and, although they occurred rarely, complications such as bleeding, pneumothorax, and tumor seeding along the needle tract have been reported. One tumor was diagnosed as RCC by percutaneous biopsy, which was an indeterminate mass when initially discovered. We could not confirm whether it was malignant, so we performed a biopsy 12 months after discovery. With imaging modality advances, we can make a more accurate diagnosis in most cases before treatment. Therefore, we consider that invasive examination such as biopsy is less useful for patients unsuitable for surgery or who refuse treatment.

We employed the greatest diameter of the tumor as an index, whereas other investigators use the tumor volume^{8–10)}. To achieve a better estimate of tumor burden, tumor volume may be better; however, we generally use the tumor diameter for treatment decisions or the prediction of prognosis in daily practice. The greatest tumor diameter is used in TNM classification. It is convenient to use the diameter and easy to recognize changes in tumor size.

As almost all RCC patients are treated surgically soon after diagnosis, the natural history of RCC has not been investigated thoroughly. The growth rates of small renal tumors have been reported to be 0.1 to 0.42 cm per year^{7–11)}, but our tumors showed slower growth than

previously reported cases (0.06 cm per year). Only 4 cases grew obviously, one tumor was reduced in size, and the remaining 10 cases did not grow at all during the observation period. The average growth rate of 4 enlarging tumors was 0.19 cm per year. The mean follow-up of the enlargement group (56 months) was longer than that of the no-growth group (26.6 months). It may be difficult to detect changes in tumor size over a short period when tumors grow very slowly, and our cases might include more benign lesions than other reported cases.

None of the patients developed metastasis during the preoperative observation period or the subsequent postoperative follow-up; other investigators reported similar results^{7–11)}. Thus a nonsurgical observation might be acceptable for elderly or comorbid patients. However, recently minimally invasive treatments such as radio frequency ablation and cryotherapy have gradually become available and can be performed safely in elderly or comorbid patients. Therefore, conservative management without treatment should be strictly indicated only for patients with severe comorbidity and short life expectancy or patients who have refused all treatment.

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和文抄録

無治療経過観察した腎腫瘍の自然経過

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虎の門病院泌尿器科

検診や他疾患の精査で画像検査を受ける機会が増加してきたのに伴い、偶然発見される小さな腎癌が増加してきている。画像上腎癌が疑われる場合、通常すぐに外科的に摘除されるが、高齢者や重篤な合併症を有する患者では手術をためらうことがある。また患者が手術を拒否する場合もある。腎癌の自然経過はよくわかっていない。われわれは画像検査で腎癌が疑われながら無治療で経過観察した、15例について検討した。CT 検査上、造影剤で造影される 4 cm 以下の腫瘍を対象とした。腫瘍発見時の平均年齢は67歳、平均腫瘍径は 22 mm、平均観察期間は38カ月だった。腫瘍の平

均増大速度は1年当たり 0.06 cm で、経過中腫瘍径が明らかに増大したのは4例のみだった。経過中3例外科的に摘除し、すべて腎癌と診断された。無治療経過観察中あるいは術後に転移が出現した症例はなかった。無治療経過観察した2例が他病死した。悪性が疑われる小さな腎腫瘍を認めても、高齢者や重篤な合併症を有する患者では、経過観察も選択肢の1つになりうると考えられた。しかし、若い患者や状態のよい患者に適応できるかは慎重に検討する必要がある。

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